

Claims 1-9, 13,14, 16-21 and 26-31 were presented for examination and Claims 1-9, 13,14, 16-21, 26, 28, 30 and 31 are now present in the case.

It is the Examiner's contention that claims 27 and 29 are directed to subject matter which is independent and distinct from that which was "originally" claimed. Moreover, since an action on the merits of the originally claimed invention has already been received, the Examiner has withdrawn Claims 27 and 29 pursuant to 37 CFR 1.42(b) and MPEP § 821.03. Although Applicants do not agree with the Examiner's contention, Claims 27 and 29 have been cancelled without prejudice to Applicants' right to file a divisional thereon.

The Examiner has rejected Claims 1-9, 13, 14, 16-21, 26, 28, 30 and 31 under 35 USC 102 (a), (b), (e) and/or (f) as being anticipated by Meier I (European Patent 199,262) and Meier II (USP 4,789,680), the latter of which is the US equivalent of the European patent for the reasons set forth in Paper No. 5, ie, the Official Action dated June 1, 2000. The Examiner again contends that since Example 4 of Meier I and Example 35 of Meier II disclose a crystalline form of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide from ethanol, said examples anticipate all of the instant claims. In this connection, the Examiner again relies on certain case law in an effort to support her position. Applicants again respectfully disagree with the Examiner's conclusion.

As indicated in Applicants' previous response, although they agree with the propositions set forth in the case law relied upon by the Examiner, it is Applicants' belief that they are inapplicable to the present fact situation. Quite simply, the Meier I and Meier II references are devoid of any mention that the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide can exist in different crystalline forms, let alone the specific crystalline forms to which the instant claims are limited. The mere disclosure of a single compound does in no way suggest the existence of a group of polymorphic forms, as alleged by the Examiner. There is clearly no class or genus of compounds suggested by the Meier references which could be held to consist of compounds that, in view of the case law relied upon by the Examiner, could anticipate any of the instantly claimed crystalline forms. Moreover, the instantly claimed crystalline forms are characterized by characteristic lines at interplanar spacings as determined by means of an X-ray powder pattern. Accordingly, neither the teachings of Meier I nor the teachings of Meier II anticipate any of the instant claims since each and every element of the instantly claimed invention is not disclosed by either the Meier I or Meier II references. See, in this connection, *Hybritech Inc. v. Monoclonal*

*Antibodies, Inc.*, 231 USPQ 81, 91 (Fed. Cir. 1986), *cert. denied*, 107 S. Ct. 1606 (1987) ("every element of the claimed invention must be identically shown in a single reference").

In view of the foregoing, the Examiner is respectfully requested to reconsider the 35 USC 102(a), (b), (e) and/or (f) rejection and withdraw it.

The Examiner has also rejected Claims 1-9, 13, 14, 16-21, 26, 28, 30 and 31 under 35 USC 103 as being unpatentable over Meier I and II (as identified above) in view of Munzel I (Progress in Drug Research, Vol. 10, pgs. 227-230, 1966) and Munzel II (Progress in Drug Research, Vol. 14, pgs. 309-321, 1970) for the reasons set forth in Paper No. 5. The Examiner again contends that since the Meier references disclose a crystalline form of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide, save for the lines with interplanar spacings of the X-ray powder pattern of said form or any other characterizing parameters, and since the Munzel references teach that compounds can exist in different polymorphic forms which retain the activity of the compounds, the instantly claimed crystalline forms would have been prima facie obvious to one skilled in the art from the combined teachings of the references. Applicants again respectfully disagree and, in view of the following arguments, believe that the 35 USC 103 rejection is significantly defective and should be withdrawn.

As indicated in Applicants' previous response, Applicants readily acknowledge that Example 4 of Meier I and Example 35 of Meier II have the same chemical formula as the compound of Claims 1 and 7, the scopes of which are directed to two different crystalline forms of said compound. However, as the court stated in re Cofer, 148 USPQ 57: "a new crystalline form of a compound would not be obvious absent evidence that the prior art suggests the particular structure or form of the compound and a suitable method of obtaining that form or structure". Accordingly, the salient question to be asked is whether the Meier references relied upon by the Examiner satisfy the strictures set forth in the Cofer decision supra? It is quite clear that one can only answer this question in the negative. Thus, no more than a cursory review of the Meier references reveals the fact that they are silent with regard to even a hint of a recognition that the specific compound alluded to above can exist in different crystalline forms, let alone contains any suggestion that different crystalline forms could or should be made or how any of the crystalline forms can be obtained. This, Applicants respectfully submit, is a critical deficiency of the Meier references. Without an obvious method of making Applicants' claimed crystalline forms, they cannot be obvious under 35 USC 103 (see, in this connection, In re Hoeksema, 58 USPQ 596). Applicants

respectfully submit that different crystalline forms of a compound are not inherent or structurally obvious unless there is a clear teaching or some chemical theory which supports this conclusion (see, in this connection, In re Grose, 201 USPQ 57). In the instant case, there is no clear teaching or chemical theory which would render either of Applicants' claimed crystalline forms and the method of obtaining them prima facie obvious.

In an effort to dispel any lingering doubts that the Examiner may have regarding the deficiency of the teachings of the Meier references to the instantly claimed crystalline forms, the Examiner's attention is respectfully invited to the enclosed documents, hereinafter referred to as Document 1 and Document 2. Document 1, entitled "Kenndaten für Praeparat CGP 33101", is dated January 20, 1987 and is signed by René Meier, the same René Meier who is the sole patentee of the two Meier references relied upon by the Examiner. Section 4 of Document 1, entitled "Polymorphism" reads as follows: "Have observations been made, which lead one to suppose that different crystal modifications exist (e.g., clear visual differences in crystal aspect when crystallized from different solvents, different melting points; variable IR spectra for presumably same degree of purity)". From this, it is clear that René Meier himself, a man skilled in the art, was unaware that CGP 33101 (aka, Example 4 of Meier I and Example 35 of Meier II) existed in different polymorphic forms. Document 2, entitled "Biopharmaceutical Data Collection - CGP 33101", is dated May 27, 1987. In the table below the section heading "Polymorphism and Hydrates" on Page 1, there is disclosed characterizing data for a single neutral compound in crystalline form and a reference to Document 1 (see the last column of the table). From this, it is clear that Document 2 is devoid of any teaching that points to the existence of different crystalline forms for CGP 33101. In brief, not only was René Meier unaware that CGP 33101 existed in different polymorphic forms at the time the earliest in the family of U.S. cases which eventually matured into USP 4,789,680 was filed (i.e., December 16, 1983), but Documents 1 and 2 clearly establish that more than three years later René Meier, a man skilled in the art, in spite of his knowledge that any compound may show polymorphism, not only doubted that CGP 33101 existed in different polymorphic forms but was not motivated to investigate the "polymorphism" aspect of CGP 33101.

As to the Munzel I and Munzel II references, neither of these references cures the deficiency of the Meier references relied upon by the Examiner. Admittedly, the Munzel references teach that compounds can exist in different polymorphic forms. However, this represents no more than what is already known in the prior art and, as indicated above, this knowledge failed to motivate René

Meier to investigate the "polymorphism" aspect of CGP 33101. Accordingly, the combined teachings of the Munzel and Meier references do not suggest the existence of Applicants' claimed crystalline forms and certainly nothing which would suggest how they can be obtained. At best, the combined teaching of the Munzel and Meier references represent an "invitation to experiment" which is insufficient under 35 USC 103. To wit, although the syntheses described in Example 4 of Meier I and Example 35 of Meier II results in the obtainment of 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide in solid form, the description is devoid of any mention of any crystal modification or mixture thereof. In fact, upon reproducing the examples, one skilled in the art would still be unaware of the existence of crystalline forms or how they can be obtained since the crystallization conditions (e.g., concentration, quality of the solvent, quality of the crude product, temperatures, type of crystallization such as seeding, change in temperatures, etc.) are absent. In addition, from the melting point set forth in said examples, no definitive conclusion can be drawn that any crystalline form was present at room temperature since, by heating, a transformation can take place. Therefore, the mere indication of the temperature does not allow for any characterization of the solid product obtained. Still further, it is not even possible to presume which crystalline form has actually melted.

In conclusion, there must be a suggestion or teaching in the prior art that the "new" crystalline forms discovered by the Applicants could or should be made, whether by manipulation of the prior art process being relied upon or by some other process. Clearly, there is nothing in the combined teachings of the Meier and Munzel references or any other prior art which would suggest or teach that crystalline forms of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide exist and that they could or should be made. Nor, more importantly, is there anything in the combined teachings of the Meier and Munzel references or any other prior art which would suggest or teach a method of making Applicants' claimed crystalline forms.

In view of the foregoing, it is clear that Applicants' claimed crystalline forms are unobvious and patentable over the combined teachings of the Meier and Munzel references. Accordingly, reconsideration and withdrawal of the 35 USC 103 rejection is respectfully requested.

Moreover, the Examiner has rejected Claims 1-9, 13, 14, 16-21, 26, 28, 30 and 31 under the second paragraph of 35 USC 112 as being "indefinite" in two respects.

First of all, Applicants again do not agree that the expression "essentially pure form" is meaningless. As indicated in Applicants' previous response, the expression is intended to mean "essentially free of any other polymorphic forms". In this connection, the Examiner's attention is respectfully directed to the fourth complete paragraph on Page 10 of the instant specification.

Secondly, Applicants do not agree that the phrase "but has defects in the crystal lattice" in Claims 7, 16-20, 30 and 31 renders said claims indefinite and their scopes unascertainable. It is clear from a reading of the specification that the phrase refers to "smaller line spacings", when compared to crystal modification A, as detected by X-ray analysis. In this connection, the Examiner's attention is respectfully directed to the third paragraph on Page 2 of the instant specification.

As to the Examiner's comment that Claims 1-9, 13, 14, 16-21, 26, 28, 30 and 31 are substantial duplicates, Applicants respectfully disagree. Claim 1 is intended to claim a specific crystalline form of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide, viz., crystal modification A, and characterizes said crystalline form with sufficient particularity. As to the other crystalline form, viz., crystal modification A', it is identical to crystal modification A, save for smaller line spacings as detected by X-ray analysis (see the discussion in the preceding paragraph). In any event, since it is Applicants' belief that the scope of Claim 1 embraces a crystalline form, with and without defects in its crystal lattice, Claim 7 as well as other claims which depend or ultimately depend on Claim 1, are properly dependent.

In view of the foregoing, the Examiner is respectfully requested to reconsider the rejection under the second paragraph of 35 USC 112 and withdraw it.

Furthermore, the Examiner has rejected Claims 1-9, 13, 14, 16-21, 26, 28, 30 and 31 under the judicially created doctrine of "obviousness-type double patenting" as being unpatentable over Claims 1-10, 14 and 20 of USP 4,789,680 (referred to above and hereinafter as Meier II) in view of Munzel I and II (as identified above).

The deficiencies of the combined teachings of Meier II and the Munzel references relative to the instant claims has been indicated above regarding the 35 USC 103 rejection and, accordingly, all of the foregoing arguments apply.

In short, there is nothing in the combined teachings of the Meier II and the Munzel references which would suggest or teach that crystalline forms of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide exist and that they could or should be made. Nor, more importantly, is there anything in the combined teachings of the Meier II and Munzel references which would suggest or teach a method of making Applicants' claimed crystalline forms.

In view of the foregoing, it is clear that Applicants' claimed crystalline forms are unobvious and patentable over the combined teachings of the Meier II and Munzel references. Accordingly, reconsideration and withdrawal of the "obviousness-type double patenting" rejection is respectfully requested.

Still further, the Examiner has rejected Claims 1-9, 13, 14, 16-21, 26, 28, 30 and 31 under the judicially created doctrine of "obviousness-type double patenting" as being unpatentable over the claims of copending U.S. Application No. 09/599,699 in view of Munzel I and II. It is the Examiner's contention that since copending U.S. Application No. 09/599,699 discloses a crystalline form of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide, viz., crystal modification B, and since the Munzel references teach that compounds can exist in different polymorphic forms, the instant claims are not patentably distinct over the claims in copending U.S. Application No. 09/599,699. Applicants respectfully disagree with the Examiner's contention and her conclusion of "obviousness".

Admittedly, copending U.S. Application No. 09/599,699 claims crystal modification B of the compound 1-(2,6-difluorobenzyl)-1H-1,2,3-triazole-4-carboxamide, as noted by the Examiner and, in fact, crystal modification C of said compound and additionally mentions the existence of crystal modifications A and A', i.e., the two crystalline forms to which the instant claims are directed. However, since copending U.S. Application No. 09/599,699 is silent with regard to any teaching as to how the specific crystalline forms of the instant claims can be prepared and since the Munzel references do not cure this defect, Applicants respectfully submit that the combined teachings of copending U.S. Application No. 09/599,699 and the Munzel references do not render any of the instant claims prima facie obvious.

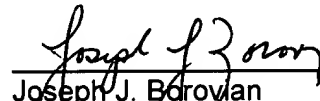
All of the rejections of record having been overcome, the instant application is deemed to be in condition for allowance, and an early notice to that effect is earnestly solicited. However, in the

event that this Amendment Under 37 CFR 1.116 is not deemed to place this application in condition for allowance, it is respectfully requested that it be entered for appeal purposes.

Since the above amendment merely involved the cancellation of claims, no additional fee is necessitated by this Amendment Under 37 CFR 1.116.

Respectfully submitted,

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Encls.: Copies of Documents 1 and 2  
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